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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/209,023	12/10/1998	VIRGINIA E. PATON	P1256R3	8941

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EXAMINER
HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
1642	27

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/209,023	PATON ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9,12,13 and 34-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9,12,13 and 34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed December 10, 2002 is acknowledged. Claims 2 and 3 were canceled. Claim 38 was added.

Claims 1, 4-9, 12, 13 and 34-38 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

3. The Information Disclosure Statements of 9/6/2001, 4/10/2002, 6/3/2002 and 6/17/2002 are present in the file; copies of signed PTO-1449 forms are attached. The references have been considered, except for some of the references listed in the IDS of 6/3/2002, which were not present in the file. The PTO-1449 form for the IDS filed 1/31/2002 is not present in the file, and the references do not appear to be either.

Claim Rejections Withdrawn:

4. The rejection of claim 13 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment to the claims.

5. The rejection of claims 1, 2, 7-9, 12, and 13 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment to the claims.

6. The rejection of claims 1, 4-9, 12-13, and 34-37 under 35 U.S.C. 103(a) as being unpatentable over **Baselga et al.**, Oncology, Vol 11, No 3, March 1997, **Norton**, Seminars in Oncology, Vol 24, No 4, Suppl 10, August 1997, **Lippman et al**, US Patent 5,578,482, November 26, 1996, **Hynes et al.** Biochemica et Biophysica Acta 1198, 1994, or **Arakawa et al**, US Patent 5,783,186, in view of **Clemons et al.**, European Journal of Cancer, Volume 33, No. 13, pages 2171-2182, November 1997, **Mosconi et al.**, European Journal of Cancer, Volume 33, Supl. 1, pages S14-S17, January 1997, **Carmichael et al.**, European Journal of Cancer, Volume 33, Suppl 1, pages S27-S30, January 1997 (Carmichael I), or **Carmichael et al.** Journal of Clinical Oncology, Vol. 13, No. 11, pages 2731-2736, November, 1995 (Carmichael II), or **Tsai et al.**, Cancer Research Vol. 56, pages 794-801, 1996 is withdrawn upon further consideration.

7. The rejection of claims 1, 4-9 and 37 under 35 U.S.C. 103(a) as being unpatentable over Hudziak et al., US Patent 5,770,195, and further in view of Clemons et al., European Journal of Cancer, Volume 33, No. 13, pages 2171-2182, November 1997, Mosconi et al., European Journal of Cancer, Volume 33, Supl. 1, pages S14-S17, January 1997, Carmichael et al., European Journal of Cancer, Volume 33, Suppl 1, pages S27-S30, January 1997 (Carmichael I), or Carmichael et al. Journal of Clinical Oncology, Vol. 13, No. 11, pages 2731-2736, November, 1995 (Carmichael II), or Tsai et al., Cancer Research Vol. 56, pages 794-801, 1996 is withdrawn upon further consideration.

8. The rejection of claims 1, 4-9, 12-13, and 37 under 35 U.S.C. 103(a) as being unpatentable over Baselga et al, Journal of Clinical Oncology, Vol 14, No 3, March 1996, in

view of Clemons et al., European Journal of Cancer, Volume 33, No. 13, pages 2171-2182, November 1997, Mosconi et al., European Journal of Cancer, Volume 33, Supl. 1, pages S14-S17, January 1997, Carmichael et al., European Journal of Cancer, Volume 33, Suppl 1, pages S27-S30, January 1997 (Carmichael I), or Carmichael et al. Journal of Clinical Oncology, Vol. 13, No. 11, pages 2731-2736, November, 1995 (Carmichael II), or Tsai et al., Cancer Research Vol. 56, pages 794-801, 1996, and further in view of in view of Hynes et al, Biochimica et Biophysica Acta, 1994, page 178 is withdrawn upon further consideration.

9. The rejection of claims 1, 4-9 and 12-13, and 34-37 under 35 U.S.C. 103(a) as being unpatentable over Baselga et al., Journal of Clinical Oncology, Vol 14, No 3, March 1996 (Baselga I), Baselga et al., Oncology, Vol 11, No 3, March 1997 (Baselga II), Norton, Seminars in Oncology, Vol 24, No 4, Suppl 10, August 1997, Lippman et al, US Patent 5,578,482, November 26, 1996, Hynes et al. Biochemica et Biophysica Acta 1198, 1994, or Arakawa et al, US Patent 5,783,186 or Hudziak et al., US Patent 5,770,195, and Clemons et al., European Journal of Cancer, Volume 33, No. 13, pages 2171-2182, November 1997, Mosconi et al., European Journal of Cancer, Volume 33, Supl. 1, pages S14-S17, January 1997, Carmichael et al., European Journal of Cancer, Volume 33, Suppl 1, pages S27-S30, January 1997 (Carmichael I), or Carmichael et al. Journal of Clinical Oncology, Vol. 13, No. 11, pages 2731-2736, November, 1995 (Carmichael II), or Tsai et al., Cancer Research Vol. 56, pages 794-801, 1996, and further in view of Maier et al., Cancer Research, Vol. 51, pages 5361-5369, 1991, or Lewis et al., Cancer Immunol. Immunother, Vol. 37, 1993, and Van Moorsel et al, Seminars in

Oncology, 42/2, Suppl 7, S717-S723, 1997, or Hansen, Ann Oncol., Vol. 7, Suppl. 1, pp29, 1996 is withdrawn upon further consideration

10. The rejection of claims 1, 4-9, 12, 13 and 37 under 35 U.S.C. 103(a) as being unpatentable over Armour et al (U.S. Patent 4,994,558; issued Feb. 19, 1991) in view of Hudziak et al (U.S. Patent 5,770,195; cited above) is withdrawn upon further consideration.

New Grounds of Rejection:

11. Claims 1, 4-9, 12, 13, 34-36 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the amendment to claim 1 introduces new matter into the specification.

The amendment to claim 1 adds the limitation that the claimed treatment be "without increase in overall adverse events, compared to therapy with gemcitabine alone". The passages in the specification and the claims pointed to by applicant do not supply the necessary support for this limitation. The specification discusses the concept of combination therapies that comprise using antibodies that bind to ErbB2, and teaches that anthracyclines in combination with antibodies that bind to ErbB2 result in a syndrome of myocardial dysfunction. (It is not clear that this is considered an adverse event. On page 47 a list of results appears to demonstrate that no overall adverse events are associated with the combination of an anti-ErbB2 antibody and either an anthracycline or paclitaxel. Yet, the specification also teaches that the combination of

an anti-ErbB2 antibody and an anthracycline results in a statistically significant increase in myocardial dysfunction). The specification teaches generally the concept of combining antibodies that bind ErbB2 with any chemotherapeutic agent that is not an anthracycline, and the working example teaches that for the combination of either an anthracycline and HERCEPTIN or placlitaxel and HERCEPTIN, that there is no statistically significant increase in overall adverse events. However, the specification does not teach methods where there is no increase in overall adverse events where the specific chemotherapeutic agent is gemcitabine. The specification fails to even contemplate one example of an adverse event that might occur during treatment with an antibody that binds ErbB2 in combination with gemcitabine. Therefore, the amendment to claim 1 introduces new matter into the specification.

12. Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the specification lacks an adequate written description of methods where an anti-ErbB2 antibody and gemcitabine are co-administered, and where the effective amounts of the anti-ErbB2 antibody and gemcitabine are lower than if the two agents had been administered as single agents.

The specification contemplates generally the concept of synergism between a chemotherapeutic agent that is not an anthracycline and an anti-ErbB2 antibody (support in original claim 12), but fails to supply support for the concept of synergism between gemcitabine and an anti-ErbB2 antibody. The support for combining gemcitabine with an anti-ErbB2

antibody in a method for treating cancer is only supported by the mention of gemcitabine in a laundry list of chemotherapeutic agents. There are no teachings or even contemplation that the specific combination of gemcitabine and an anti-ErbB2 antibody in a method for treatment, where the amounts of each agent is less than the amounts of each agent when administered singly. While it may not be surprising that synergism may occur, and, therefore, a method as claimed could be made, the specification does not present evidence that applicant was in possession of the claimed invention at the time of filing. The one example provided by the specification concerning chemotherapy in combination with an anti-ErbB2 antibody fails to demonstrate synergism. Thus, the specification lacks even one example for the general concept synergism, and therefore, fails to provide any support for the specific combination of gemcitabine and an anti-ErbB2 antibody.

13. Claims 1, 4-9, 12, 13, 34-36 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite, because the scope of the phrase "overall increase in adverse events" is unclear. As discussed above, on page 47 of the specification, a list of results appears to demonstrate that no overall adverse events are associated with the combination of an anti-ErbB2 antibody and either an anthracycline or paclitaxel. Yet, the specification also teaches that the combination of an anti-ErbB2 antibody and an anthracycline results in a statistically significant increase in myocardial dysfunction. Because the development of myocardial dysfunction would

appear to be an adverse event, the teachings of the specification call into question the scope of the phrase "overall increase in adverse events".

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
February 24, 2003

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